Docket No. TPI5013USPCT6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Mark Tawa, et al.	Confirmation No.:	4554
Application No.:	10/541,216	Group Art Unit:	1627
Filing Date:	June 29, 2005	Examiner:	Claytor, D.R.
For:	PHARMACEUTICAL COMPOSITIONS WITH IMPROVED DISSOLUTIONS		

DECLARATION UNDER 37 C.F.R. § 1.132

I, Mark Tawa, a named inventor in the above-identified patent application declare that:

1. I have read and understand the rejection of claims 46-68 under 35 U.S.C. § 102 in the December 23, 2010 final Office Action. In particular, I understand that claims 46-48 are rejected as being anticipated by Remenar et al. (U.S. Published Application No. 20060052432).

2. I understand that the Examiner asserts that:

    a. Remenar et al. claims priority to U.S. Application Serial No. 60/427,086, which was filed on November 15, 2002;

    b. U.S. Application Serial No. 60/427,086 discloses a sodium salt form of celecoxib.

    c. U.S. Application Serial No. 60/427,086 discloses that a poloxamer can act as a precipitation retardant.

    d. Priority for Remenar et al. goes to at least November 15, 2002.

    (See final Office Action at page 2).

3. I and my co-inventors were in possession of the invention claimed in the above-identified patent application prior to November 15, 2002, the earliest filing date for Remenar et al. This is evidenced by the contents of the attached laboratory notebook pages.

4. The dates on each of the laboratory notebook pages, which have been redacted, were all prior to November 15, 2002.

5. The laboratory notebook pages demonstrate that I and my co-inventors were in possession of the invention recited in claims 46-68 prior to the November 15, 2002 filing date. More particularly, the laboratory notebook pages demonstrate that I and my co-inventors prepared:

   A pharmaceutical composition comprising a salt form of celecoxib and a poloxamer. (See Laboratory Notebook No. 129, Pages 14-18).

   A pharmaceutical composition comprising a salt form of celecoxib and an enhancer (e.g., hydroxypropylcellulose and hydroxypropylmethylcellulose). Laboratory Notebook No. 114, Pages 100-102

The declarant further states that the above statements were made with the knowledge that willful false statements and the like are punishable by fine and/or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statement may jeopardize the validity of the above-identified patent application or any patent resulting therefrom.

Date: 16 March 2011

Mark Tawa
(Signature of Mark Tawa)

Attachments:
Laboratory Notebook No. 129, Pages 14-18
Laboratory Notebook No. 114, Pages 100-102

NOTEBOOK NO. 114

ISSUED TO Mark Tanis

ON 7/1/02

DEPARTMENT Solid State Chemistry

RETURNED

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Project No. _____

TITLE Cel Nca + Vit E TGPS Mixtures

Book No. 114

From Page No.

Celecoxib Na - MT-114-94-A

Vitamin E TGPS - Eastman Lot 90001000

Poloxamer 237 - Spectrum Lot PE0487

Hydroxypropyl cellulose 100,000 - Hercules Lot 402J48

Hydroxypropyl methylcellulose (80-120 cps) - Aldrich Lot 10768HU

" (15,000 cps) - Aldrich Lot 01929CG

Avicel (microcrystalline cellulose) PH 200 - FMC Lot MC-361

1) Vitamin E TGPS - 103.45 mg
HPC - 99.59 mg
Celecoxib Na - 112.4 mg

2) Vitamin E TGPS - 100.34
HPMC (80:120) - 99.96
Celecoxib Na - 110.4

3) Vitamin E TGPS - 103.72
HPMC (15,000) - 99.76
Celecoxib Na - 111.3

4) Vitamin E TGPS - 102.19
Avicel (PH 200) - 101.34
Celecoxib Na - 110.8

- Mixtures 1-4 were made via heating of Vitamin E TGPS to melt it (by heat gun); Celecoxib Na added and mixed together followed by 3rd excipient
- all steps excluded stirring
- mixtures were cooled and weighed out for dissolution assays

To Page No. 101

SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
Mark Tann	11/4/02	Lisa A. Lapp-Thurlo	12/5/02

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TITLE Cel Na + Vit E TOPS Mixtures (cont) Book No. 114

From Page No. 100

Assay Vial 1 (95.4 mg)

HPLC Vial	time
9	1:01
10	3:00
11	5:00
12	10:02
13	20:12
14	30:00

Assay Vial 2 (94.2 mg)

HPLC Vial	time
15	1:00
16	3:00
17	5:05
18	10:01
19	20:00
20	30:00

- still hasn't completely broken up yet @ 30 min

~~to~~ small chunk not dissolved — liquified @ 30 min

Assay Vial 3 (94.3 mg)

HPLC Vial	time
21	1:00
22	3:18
23	5:00
24	10:02
25	20:00
26	30:00

Assay Vial 4 (93.5 mg)

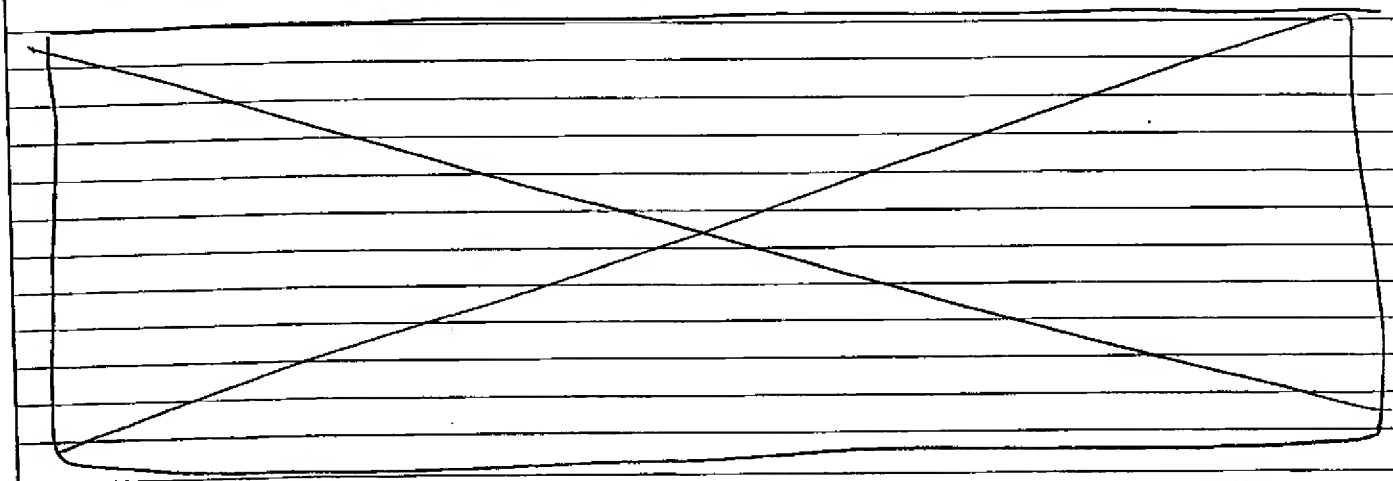
HPLC Vial	time
27	1:00
28	3:05
29	5:10
30	10:11
31	20:00
32	30:00

Shook

- large clump stays undissolved

- solid dispersed throughout mixture

- all assays run w/ 15 mL of SGF (Zhang Zhang)
- 0.75 mL aliquots removed and filtered through 0.2 μm PVDF syringe filters
- the first ~0.6 mL are discarded and the remaining filtrate is collected
- from the filtrate is collected ~~0.5~~ 50uL which is quenched w/ 0.70 mL of MeOH (15 x dilution)



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SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
Mark Tann	11/14/02	Lisa A. Sappetulo	12/5/02

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Project No. _____

TITLE HPLC data for p 100 - 101

Book No. 114

From Page No. 101

Mark Taura

ATRR0230.xls

data

Transform Pharmaceuticals

Analytical Testing Data

ATR/R #:	230			
HPLC sample	Name	Time Point	Dilution Factor	Conc mg/mL
1	1:1 Vit E TGPS:CelNa Content uniformity		1	0.091
2	1:1 Vit E TGPS:CelNa Content uniformity		1	0.123
3	1:1 Vit E TGPS:CelNa Content uniformity		1	0.068
4	1:1 Vit E TGPS:CelNa Content uniformity		1	0.072
5	1:1 Vit E TGPS:Cel Content uniformity		1	0.112
6	1:1 Vit E TGPS:Cel Content uniformity		1	0.096
7	1:1 Vit E TGPS:Cel Content uniformity		1	0.137
8	1:1 Vit E TGPS:Cel Content uniformity		1	0.110
9	1:1:1 Vit E TGPS:HPC:CelNa (2 mg/ml API)	1 min	15	0.073
10	1:1:1 Vit E TGPS:HPC:CelNa (2 mg/ml API)	3 min	15	0.200
11	1:1:1 Vit E TGPS:HPC:CelNa (2 mg/ml API)	5 min	15	0.449
12	1:1:1 Vit E TGPS:HPC:CelNa (2 mg/ml API)	10 min	15	0.798
13	1:1:1 Vit E TGPS:HPC:CelNa (2 mg/ml API)	20 min	15	1.254
14	1:1:1 Vit E TGPS:HPC:CelNa (2 mg/ml API)	30 min	15	1.520
15	1:1:1 Vit E TGPS:lv HPMC:CelNa (2 mg/ml API)	1 min	15	0.011
16	1:1:1 Vit E TGPS:lv HPMC:CelNa (2 mg/ml API)	3 min	15	0.196
17	1:1:1 Vit E TGPS:lv HPMC:CelNa (2 mg/ml API)	5 min	15	0.381
18	1:1:1 Vit E TGPS:lv HPMC:CelNa (2 mg/ml API)	10 min	15	0.672
19	1:1:1 Vit E TGPS:lv HPMC:CelNa (2 mg/ml API)	20 min	15	1.202
20	1:1:1 Vit E TGPS:lv HPMC:CelNa (2 mg/ml API)	30 min	15	1.186
21	1:1:1 Vit E TGPS:hv HPMC:CelNa (2 mg/ml API)	1 min	15	0.004
22	1:1:1 Vit E TGPS:hv HPMC:CelNa (2 mg/ml API)	3 min	15	0.018
23	1:1:1 Vit E TGPS:hv HPMC:CelNa (2 mg/ml API)	5 min	15	0.006
24	1:1:1 Vit E TGPS:hv HPMC:CelNa (2 mg/ml API)	10 min	15	0.003
25	1:1:1 Vit E TGPS:hv HPMC:CelNa (2 mg/ml API)	20 min	15	0.003
26	1:1:1 Vit E TGPS:hv HPMC:CelNa (2 mg/ml API)	30 min	15	0.012
27	1:1:1 Vit E TGPS:Avicel PH 200:CelNa (2 mg/ml API)	1 min	15	0.298
28	1:1:1 Vit E TGPS:Avicel PH 200:CelNa (2 mg/ml API)	3 min	15	0.715
29	1:1:1 Vit E TGPS:Avicel PH 200:CelNa (2 mg/ml API)	5 min	15	0.617
30	1:1:1 Vit E TGPS:Avicel PH 200:CelNa (2 mg/ml API)	10 min	15	0.190
31	1:1:1 Vit E TGPS:Avicel PH 200:CelNa (2 mg/ml API)	20 min	15	0.137
32	1:1:1 Vit E TGPS:Avicel PH 200:CelNa (2 mg/ml API)	30 min	15	0.127

Mark Taura

- good solubility profiles seen for HPC and HPMC (low viscosity)
- going to carry forward w/ one of these two formulations

To Page No.

SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
Mark Taura	11/5/02	Lisa A. Scappettone	12/5/02

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NOTEBOOK NO. _____

ISSUED TO Héctor Guzmán

ON _____

DEPARTMENT Solid-State Chemistry

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Project No. _____

TITLE TPI-336 Na w/ Various Poloxamers : Dissolution from Solid-state

Book No. _____

From Page No.

Goals: Test various solid-state ratios of Poloxamer in the solid state w/ TPI-336 Na. Measure dissolution properties

Design:

Excipient: ① Poloxamer 237 - Spectrum # P1167, Lot # PE0487, ② Poloxamer 407 - Spectrum P1166, Lot QP0478

③ Poloxamer 338 Spectrum P1172, Lot # PH0500

④ PVP K30 - Spectrum P1454, Lot # LOB1180

SGF : pH 1.7 adjusted - diluted 5x - 15 mL volume per sample for 2mg API/unit dose HT-114-39A

Group Assayed	Excipient / mg	Ratio	API (mg)	#	Assay Vial (mg)	Grind Type
1	Poloxamer 237/83.7	2:1	46.5	1	#1, 95.2	chunky; slight graying
2	Poloxamer 237/86.2	1:1	79.6		#2, 65.5 #3, 65.5	loose powder
3	Poloxamer 338/160.6	2:1	92.4		#4 153.8 #5 153.7	powder
	PVP / 160.4	2:1	—			
4	Poloxamer 338/181.3 +161.6 343.2	2:1 1:1	93.5		#6, 163.4 #7, 64.5	powder
5	Poloxamer 407/81.8	1:1	94		#8, 65.5	
6	Poloxamer 188/ Done by Rick	1:1	Performed by Poe R.		#9, 64.8	Powder

Note: Some samples were performed and stored by Mark Tawa, Z.T. or Poe. For the samples shown below are samples were filtered by Hector Guzman using a 0.2 um PVDF filter.

Assay Vial #1		Assay Vial #2		Assay Vial #3		Assay Vial #4	
Time	HPLC #	Time	HPLC #	Time	HPLC #	Time	HPLC #
40	1	41	6	57	11	0:42	16
1:35	2	1:49	7	1:45	12	1:30	18
3:00	3	2:53	8	2:57	13	2:58	17
4:57	4	4:58	9	4:55	14	4:59	19
10:00	5	10:00	10	9:54	15	9:56	23

Assay Vial #7		Assay Vial #8		Assay Vial #9	
Time	HPLC #	Time	HPLC #	Time	HPLC #
0:46	20	0:44	25	0:37	30
1:29	21	1:28	26	1:31	31
2:57	22	2:56	27	3:00	32
4:56	24	4:58	29	4:59	34
9:55	28	9:58	33	9:59	35

For sample collection, the sample procedure shown in page 8, items ② - ⑤ were followed.

extra notes: 20 mL scintillation vials were used and small stir bars were used.

The data from HPLC is stored under File name ATKR02199

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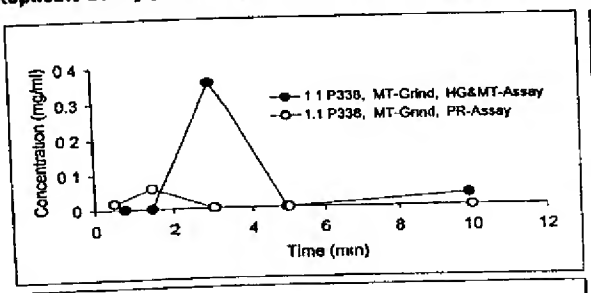
[signature]	10/21/02	Jeanie C.	1-2-03

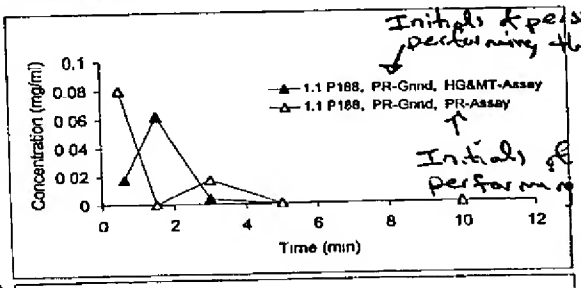
Project No. _____

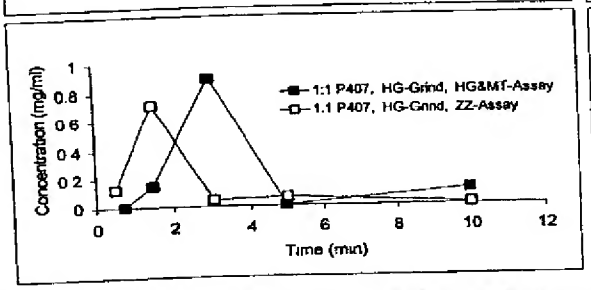
TITLE _____ Book No. _____

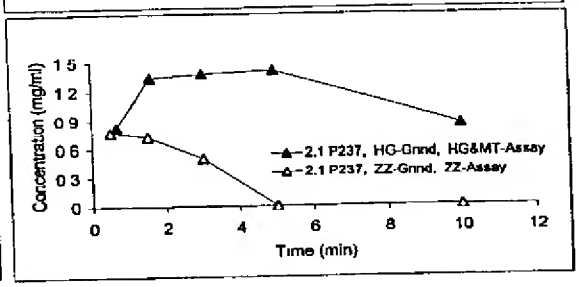
From Page No. 14

Replicate assay performed using different 1) researchers, and 2) sized stir bars

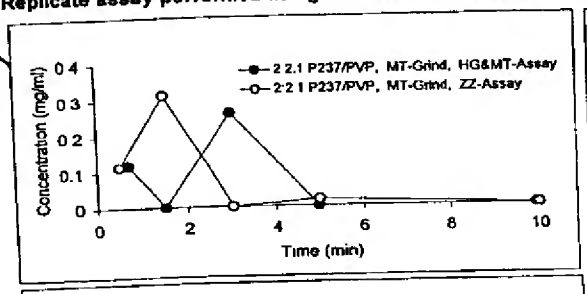


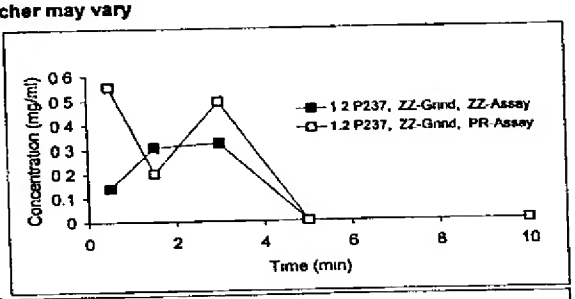


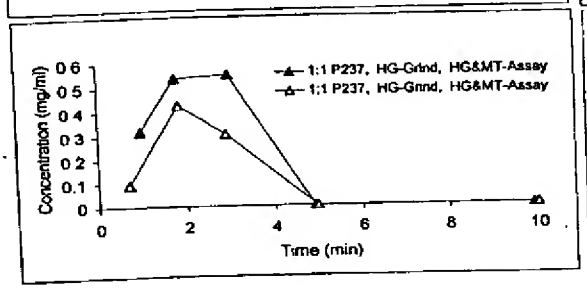


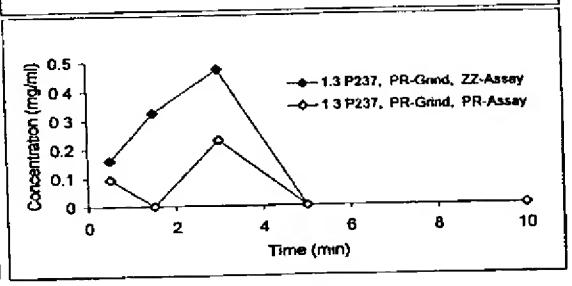


Replicate assay performed using same size stir bars; researcher may vary









Comments: In general the duplicate runs were very inconsistent among the replicates. Possible reasons are the following:

① Inconsistent grinds.

② Different stir bars were used.

- when different sized stir bars were used (ZZ and PR used large stir bars; MT + HG used small) a shift in the maximum conc. was observed.
- when the same stir bar was used, no shift was observed among the replicates

To Page No.

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	12/22/02	Jamie Cheng	1-2-13

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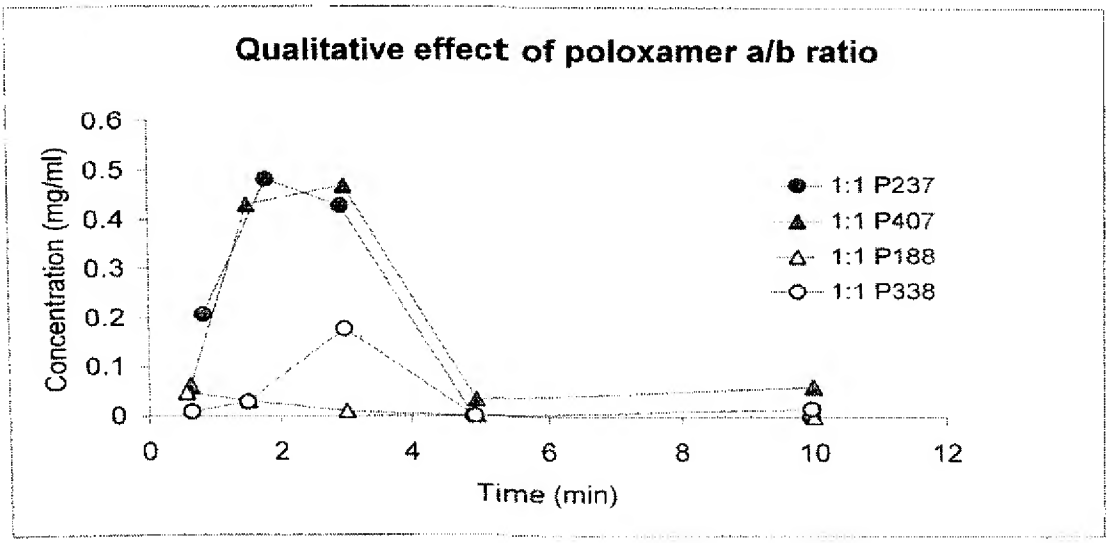
Poloxamer	Physical form	a	b	Average molecular weight	Percent a	Percent b	Ratio a/b
124	Liquid	12	20	2090-2360	0.38	0.63	0.60
188	Solid	80	27	7680-9510	**0.75**	**0.25**	2.96
		64	37	6840-8830			1.73
338	Solid	141	44	12 700-17 400	**0.76**	**0.24**	3.20
		101	56	9840-14 600			1.80

$HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_aH$



Notes:
1. Average dataset between two replicate measurements
2. Shift effect with respect to time (i.e., maximum conc.) have been ignored.

For further analysis, Poloxamers having similar percent A and percent B concentration were compared against other poloxamers this data represent data shown in page 15 that was averaged. Because of the previously observed shifts, only qualitative information can be extracted from this figure. As shown, it seem that higher % B and lower percent A results in higher concentration of TP1336 Na over time.

To Page No.

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	10/22/02		1-2-03

Project No. _____

TITLE TPI-336Na Dissolution study

Book No. _____

From Page No.

Goal: Test effect of grind API/excipient and stirring bar size on dissolution of TPI-336Na

Design

Excipient: ① Poloxamer 237 - Spectrum #P1167, PEO 87

API Dose 2mg/mL TPI336Na - MT_114_89A

SGF adjusted pH 1.7, diluted 5x with DI H2O

Methods

Three API Mixtures

③ Mixture 3 - Heavy Grind

- Pre-Grind Poloxamer 237 to fine particle size (i.e., 1 min) - 40.1 mg
- Add TPI-336Na - 92 mg
- Grind for 10 min
- Dispense into Assay Vials 7 + 8

② Mixture 2 - Light Grind

- Pre-grind Poloxamer 237 to fine particle size (i.e., 1 min) - 100.1 mg
- Add TPI-336Na - 231.5 mg
- Dispense into Assay vials 3-6

① Mixture 1 - made by Mark Tawa - Notebook #114, page 90. (No Grind)

- Same Ratio
- Dispense into assay vials 1-2.

Table of Assay Vials

Assay Vial	Weight (mg)	Vol (mL)	Grind	Appearance	Stir Bar
1	50	15	None	Loose Powder	small
2	50.5	15	None	↓	small
3	48.1	~~14.7~~ 14.5	Light	↓	small
4	48.7	~~14.7~~ 14.7	Light	↓	small
5	47.3	~~14.5~~ 14.7	Light	↓	large
6	48.8	~~14.9~~ 14.7	Light	↓	large
7	46.3	14.0	Heavy	Chunky	small
8	45.7	13.8	Heavy	Chunky	small

Assay Vial #1		Assay Vial #2		Assay Vial #3		Assay Vial #4	
Time	HPLC #	Time	HPLC #	Time	HPLC #	Time	HPLC #
~~57~~ 45	1-1	:38	2-1	:32	3-1	:27	4-1
1:55	1-2	1:45	2-2	1:14	3-2	1:25	4-2
2:55	1-3	2:44	2-3	2:24	3-3	2:36	4-3
3:40	1-4	3:45	2-4	3:10	3-4	3:43	4-4
4:56	1-5	4:54	2-5	4:28	3-5	4:55	4-5
9:59	1-6	10:01	2-6	9:59	3-6	9:52	4-6

To Page No.

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	10/22/02	Jeanie Chang	1-2-03

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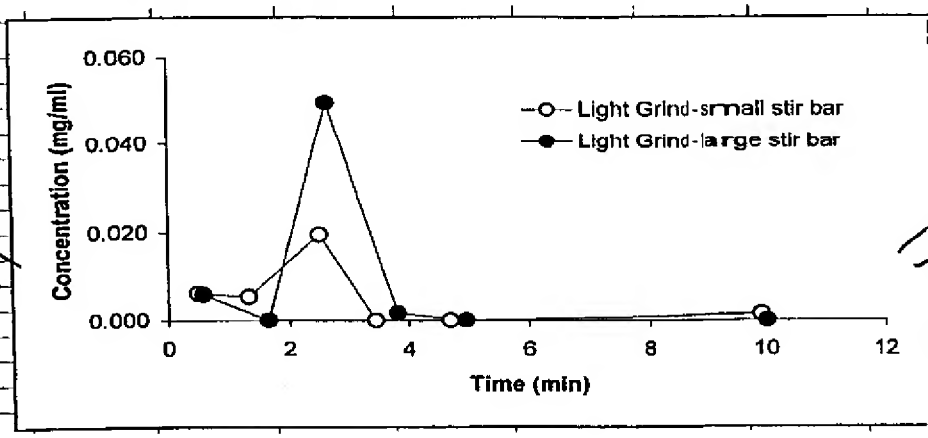
Project No.

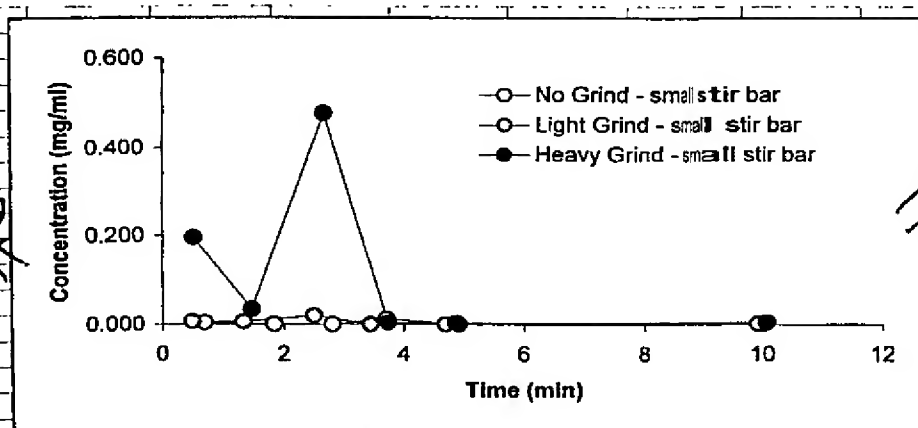
Book No.

TITLE

From Page No. 17

Assay Vial #5		Assay Vial #6		Assay Vial #7			Assay Vial #8	
Time	HPLC #	Time	HPLC #	Time	HPLC #		Time	HPLC #
27	5-1	42	6-1	33	7-1	cloudy	28	8-1
1:29	5-2	1:49	6-2	1:32	7-2	little	1:24	8-2
2:29	5-3	2:45	6-3	2:42	7-3	cloudy	2:36	8-3
3:40	5-4	3:57	6-4	3:35	7-4	clear	3:53	8-4
4:54	5-5	5:00	6-5	4:47	7-5	clear	4:58	8-5
10:00	5-6	10:02	6-6	10:08	7-6		10:01	8-6





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TP1-336 / ATRR / Dissolution.

To Page No.

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[signature]	10/23/02	[signature]	1-2-03